

Coronary artery bypass grafting in chronic renal failure and hemodialysed patients: Ten years of experience

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Abstract

Aim: To evaluate the early and long-term survival and morbidity, preoperative and operative predictors in chronic renal failure and hemodialysed patients.

Methods: From January 2007 to June 2016, 244 patients with Chronic Renal Failure (Study Group) underwent myocardial revascularization. They were divided in Group I (n=56), hemodialysed and Group II (n=188) non hemodialysed. Mean age (Group I) was 63.4±6.5 years (range 53-68) and 66.5.4±7 years (range 54-71) (Group II).

Results: The total hospital mortality in the Study Group was 17 (7%). Six (10.5%) patients died in Group I versus 11 (5.85%) in Group II (p=Ns). The postoperative complications were significantly higher in Group I versus Group II (p=0.032). Multivariate analysis revealed cerebrovascular disease (p=0.022), myocardial infarction (p=0.011), LVEF (p=0.007) and renal failure duration (p=0.01) as strong predictors for poor survival in non-hemodialysed patients. LVEF<35% (p=0.01) and HD duration (p=0.007) were identified as predictors for late mortality in hemodialysed patients. The 1, 3 and 5 years survival was, 90%, 76% and 68% in Group I and 95.5%, 86% and 81% in Group II (p=0.004).

Conclusion: Chronic renal failure patients may undergo myocardial revascularization with acceptable postoperative short and long-term mortality and morbidity. The hemodialysed patients undergoing myocardial revascularization are at a substantial risk of experiencing postoperative major morbid events and poor late survival.

Keywords: coronary artery bypass grafting, end-stage renal failure, hemodialysis.

Introduction

Coronary artery disease is the leading cause of death in patients with chronic renal failure (CRF) (2). Numerous reports (1-14) have described the outcome of cardiac surgery in CRF non hemodialysed (HD) and HD patients, demonstrating acceptable results. The cardiac operation, in these groups of patients, is considered necessary to improve life quality and prolong life expectancy (1-5). The operative risk has been significantly higher in HD patients compared to the general cardiac patient population (6), and long-term survival has been relatively low (2,5). Such results have been attributed to a multitude of coexisting noncardiac disorders (1), to the pathologic consequences of the renal disease and dialysis-inclusive infective endocarditis (3), to advanced cardiac disease (1) and older age (7). Cardiopulmonary bypass in CRF patients poses a special problem because of the enormous fluid shifts in the various parts of the body and, in addition, anemia and bleeding diathesis can complicate the peri and postoperative course. Recent studies demonstrated a significant improvement of perioperative and long-term survival in relatively small series of well-selected HD patients (1,5,8,9), therefore CABG in HD patients remains a debated issue. The aims of the present study were to evaluate the early and mid-term outcome of HD and CRF non HD patients undergoing CABG, the comorbid features in both these groups of patients and preoperative predictors for poor survival.

Methods

Between January 2007 and June 2016, 244 consecutive CRF patients (Study Group) underwent CABG. The control group consisted in 244 randomized sex, LVEF, type of operation and age-corrected patients with normal renal function (Table 1).

- *Patient population.* The Study Group patients were divided in: Group I (n=56) HD patients and Group II (n=188) CRF non HD patients with a creatinine >1.6gm/dl for more than 6 months before surgery. All Group I patients received HD for at least

1 month before operation. Mean age in Group I was 63.4 ± 6.5 years versus 65.4 ± 7 years in Group II (Table 2). Renal failure in Group I was attributed to the following pathologic disorders: polycystic disease of the kidney (n=8), SLE (n=6), chronic GNF (n=7), vascular renal disease (n=6), toxic (n=3), CPN (n=7), diabetic nephropathy (n=8), lithiasis (n=4), nephrosclerosis (n=1), unknown (n=6). 2 patients had undergone renal transplantation with subsequent failure of the donor kidney.

- *Cardiac catheterization.* All patients underwent coronary angiography before surgical procedure (Table 2). Calcification score was represented by the sum of all involved coronary artery segments following the AHA classification, confirmed by fluoroscopy.

- *Renal Dialysis.* All cardiovascular procedures were done while patients were on maintenance Hemofiltration. The mean preoperative duration of dialysis in Group I varied widely (range 6 months to 9.8 years). The preoperative level of BUN, was 123 ± 7.8 mg/dL and elevated creatinine levels 7.5 ± 0.7 mg/dL. The perioperative dialysis program consisted in the following procedures: dialysis the evening before operation, hemofiltration during the cardiopulmonary bypass, and resumption of dialysis the 1st or 2nd day after operation.

- *Operative data.* CABG was performed using cardiopulmonary bypass and moderate systemic hypothermia. Standard ascending aorta and right atrial cannulation were performed in 233 patients. 11 patients underwent femoral/axillary artery cannulation because of porcelain aorta. Intermittent cold antegrade and retrograde blood cardioplegia was used in all pts. 4 patients (Group I) underwent mitral valve surgical repair due to mitral regurgitation. It were used 178 LIMA, 41 RIMA; 11 Radial Artery. The average cross-clamping time was 83 minutes and the average CPB time was 115 minutes.

- *Follow-up.* Data were collected from patients medical records, from questionnaires sent to physician's telephone interviews. The actuarial

survival at 1, 3 and 5 years after CABG were calculated.

- *Definitions.* Hospital mortality was defined as death for any reason occurring within 30 days after operation. Perioperative myocardial infarction (AMI) was defined as the appearance of new Q-waves or significant loss of R-wave forces peak creatine phosphokinase MB fractions greater than 10% of total CK. Low cardiac output syndrome was defined as a cardiac index $<2.0\text{l/min/m}^2$, requiring pharmacological support and/or IABP insertion. Neurological complication was defined as any transient or permanent neurological deficit that developed following surgery. Gastrointestinal complications include confirmed diagnosis of upper and lower gastrointestinal hemorrhage, intestinal ischemia, acute cholecystitis and pancreatitis. Postoperative bleeding was defined as re-thoracotomy for hemorrhage.

- *Statistical analysis.* Group statistics were expressed

as mean \pm 1 SD. Mann-Whitney test was used for continuous variables; Wilcoxon's signed rank test was used for comparing the pre and postoperative variables within the same group of pts. Fisher's exact test was used for the nonparametric variables. Long-term survival rates were calculated using the Kaplan-Meier method and statistical significance was calculated by the log rank test. The step-wise logistic regression analysis was made for identifying independent predictors for survival. Significance between data was considered achieved when $p < 0.05$.

Results

The preoperative data were compared. The incidence of preoperative non cardiac and cardiac features resulted to be significantly higher in the Study Group than the Control Group (Table 1).

Table 1. Preoperative profile of chronic renal failure patients versus patients with normal renal function undergoing coronary artery bypass grafting procedure

VARIABLE	Study group (n=244)	Control group (n=244)	P-value
Diabetes	79 (32.4%)	44 (18%)	0.001
Hypertension	120 (49.2%)	78 (32%)	0.001
Hypercholesterolemia	62 (25.4%)	38 (15.6%)	0.015
Dislipidemia	32 (13%)	18 (7.4%)	Ns
CVD	60 (24.6%)	37 (15.2%)	0.013
PVD	97 (39.8%)	54 (22%)	0.001
COPD	45 (18.5%)	28 (11.5%)	Ns
Peptic ulcer	49 (20%)	31 (12.7%)	Ns
AMI	107 (38.5%)	73 (30%)	0.002
Arrhythmias	69 (28.3%)	25 (10.3%)	0.001
NYHA 3-4	29 (11.2%)	8 (3.3%)	0.001
Triple vessel disease	190 (77.8%)	159 (65.2%)	0.001
Calcification score >3	94 (38.5%)	43 (17.6%)	0.001
Left main trunk stenosis $>50\%$	52 (21.3%)	32 (13%)	0.023
Occlusion of at least one coronary artery	49 (20%)	23 (9.4%)	0.001

CVD-cerebrovascular disease; PVD-Peripheral vascular disease, COPD-Chronic obstructive pulmonary disease, AMI-Acute Myocardial Infarction.

The preoperative non-cardiac and cardiac features were compared between Group I and II (Table 2). In Group I we found a significantly higher incidence of: diabetes ($p=0.017$), hypertension ($p=0.001$), hypercholesterolemia ($p=0.028$), preoperative AMI ($p=0.001$), arrhythmias ($p=0.001$). The preoperative

angiography in Group I versus Group II revealed: triple vessel disease ($p=0.011$), LMCA stenosis $>50\%$ ($p=0.015$), coronary calcification score >3 ($p=0.001$) and occlusion of at least one coronary artery ($p=0.017$) (Table 2).

Table 2. Preoperative data analyses between Group I and Group II

Variables	Group I (N=56)	Group II (N=188)	P
Age	63.4±6.5	65.2±7.3	Ns
Diabetes	26 (46.4%)	53 (28.2%)	0.017
Hypertension	39 (69.6%)	81 (43%)	0.001
Hypercholesterolemia	21 (37.5%)	41 (21.8%)	0.028
Dislipidemia	7 (12.5%)	25 (13.3%)	Ns
Smoking	24 (42.8%)	99 (52.7%)	Ns
Family History	18 (32%)	45 (24%)	Ns
Cerebrovascular disease	23 (41%)	37 (19.7%)	0.002
Peripheric vascular disease	21 (37.5%)	76 (40.4%)	Ns
Peptic ulcer	16 (28.6%)	33 (17.6%)	Ns
Neoplasms	7 (12.5%)	11 (5.85%)	Ns
Chronic obstructive pulmonary disease	14 (25%)	31 (16.5%)	Ns
Acute myocardial infarction	40 (71.4%)	67 (35.6%)	0.001
Pulm. Hypertension	14(25%)	20 (10.6%)	0.012
Arrhythmia	28 (50%)	41 (21.8%)	0.001
Congestive heart failure	9 (16%)	20 (10.6%)	Ns
Mitral valve regurgitation	8 (14.3%)	26 (13.8%)	Ns
Triple vessel disease	51(91%)	139 (74%)	0.011
Left main trunk stenosis $>50\%$	19(34%)	33(17.6%)	0.015
Calcified lesions of coronary arteries	41 (73.2%)	53 (28.2%)	0.001
>1 total vessel obstruction	18 (32%)	18 (32%)	0.017

The hospital mortality in Group I and II were 6 (10%) patients and 11 (6%) patients respectively (p : non-significant). The causes of death were cardiac 9, infectious 4, intestinal infarction 2, respiratory 1, technical 1.

The incidence of postoperative morbidity was significantly higher in Group I versus Group II, 33 (67.3%) patients and 92 (49%) patients respectively ($p=0.032$). There were 70 (56%) cardiac complications, 20 (16%) neurological, 49 (39%) pulmonary, 23 (18.4%) gastrointestinal and 49 (39%) infectious (Table 3). Cardiac complications included 44 (63%)

arrhythmias, 3 (4.3%) cardiac arrest, 15 (21.5%) LCOS, 7 (10%) cardiac tamponade, 1 (1.4%) aortic rupture. Neurological complications included 13 (65%) cerebrovascular accident, 4 (20%) encephalopathies, 3 (15%) motor dysfunction. Pulmonary complications included 8 (16.3%) respiratory failure, 3 (6%) pulmonary embolus, 22 (45%) pleural effusions requiring tube thoracostomy drainage, 7 (14.3%) hemoptysis episodes, 2(4%) aspiration pneumonia, 4 (8%) respiratory arrest, 3 (6%) atelectasis requiring bronchoscopy. Infectious complications included 7 (14.3%) sepsis syndrome, 10 (20.4%) urinary

infections, 18 (37%) pneumonias, 2 (4%) aspergillosis, 1 (2%) candida esophagitis, 2 (6%) sinusitis requiring ENT management, 5 (10%) sternal and/or leg wound infections. Gastrointestinal complications included 3 (13%) acute pancreatitis, 12 (52%) bleeds (8 upper

and 4 lower), 4 (17.4%) cholecistitis requiring surgical intervention, 1 (4.4%) intestinal infarction, 3 (13%) peritonitis. 7 patients required reoperation for mediastinal bleeding.

Table 3. Postoperative complications in hemodialysed and chronic renal failure non hemodialysed patients undergoing coronary artery bypass grafting procedure

	Total Morbidity	Cardiac	Neurological	Pulmonary	Gastrointestinal	Infectious
Group I	33 (59%)	19	4	13	8	16
Group II	92 (49%)	51	16	36	15	33
Total		70	20	49	23	49

The intensive care unit stay was significantly higher in Group I versus Group II ($p<0.001$). The necessity of inotropes' use was significantly higher in the Study Group, 92 (38%) compared to the Control Group 64 (29%) patients ($p=0.027$). The postoperative creatinine level in Group II was significantly higher versus the preoperative level ($p<0.001$), 3.6 ± 1.3 mg/dl and 2.5 ± 1.1 mg/dl respectively. 64 (29%) patients

(Group II) necessitated hemofiltration in the postoperative course. The use of HD in the postoperative course was significantly higher in the Study Group versus the Control Group (5.5%) ($p<0.001$). 18 (28%) patients from the postoperative hemodialysed CRF patients ($n=64$) necessitated permanent HD (Table 4).

Table 4. Postoperative variables

	ICU STAY (days)	IABP	Inotropes	LVAD	Postoperative Creatinine	Postoperative ultrafiltration
Group I	9 ± 5.7	8 (14.3%)	23 (41%)	1 (1.8%)		56 (100%)
Group II	4 ± 2.3	18 (9.5%)	69 (31.5%)	3 (1.4%)	3.6 ± 1.3	64 (29%)

ICU-Intensive Care Unit, IABP-Intra Aortic Balloon Pump, LVAD-Left Ventricular Assist Device.

The univariate analysis revealed a series of predictors for in-hospital mortality in CRF non HD patients (Table 5). All the preoperative and perioperative variables were analysed. The univariate analysis identified the following as predictors of late mortality: age ($p=0.04$), cerebrovascular disease ($p=0.01$), LVEF<35% ($p=0.007$), CRF duration ($p=0.002$). The multivariate analysis identified cerebrovascular disease ($p=0.022$), preoperative AMI ($p=0.011$), LVEF<35% ($p=0.007$), and CRF duration ($p=0.01$) as independent predictors for overall survival.

The univariate analysis in HD patients revealed the presence of cerebrovascular disease ($p=0.04$), LVEF<35% ($p<0.001$) and HD duration ($p=0.0017$)

as strong predictors for in-hospital mortality. LVEF<35% ($p=0.01$) and HD duration ($p=0.007$) were identified as predictors for late mortality. Multivariate analysis was not employed due to an insufficient number of deaths.

The mean follow-up time of the 227 survivors was 37 months (range 5 to 93 months). Actuarial survival rates at 1, 3, 5 years including all deaths in Group I ($n=50$) were, 90%, 76% and 68% and in Group II ($n=177$) were 95.5%, 86% and 80.7%. The overall survival at follow-up was significantly higher in Group II versus Group I ($p=0.004$). The overall mortality at follow-up was 22 patients in Group I and 34 patients in Group II. In Group I, 3 of the late deaths were

Table 5. Univariate analysis of pre and perioperative data between survived and deceased chronic renal failure patients undergoing coronary artery bypass grafting procedure

Variable	Failed (N=11)	Successful (N=177)	P
Age	69±4	65±6	0.03
Hypertension	10	71	0.003
Cerebrovascular disease	7	30	0.001
Chronic obstructive pulmonary disease	5	26	0.024
Preoperative myocardial infarction	8	59	0.02
Arrhythmia	6	35	0.02
Left ventricular ejection fraction	34.8±3.5	38.6±3.7	0.001
Chronic renal failure duration	6±1.5	3±1	0.001
Emergency	5	17	0.002

undergone total arterial myocardial revascularization versus 19 patients who undergone CABG using saphenous veins and LIMA ($p=0.011$). The causes of late mortality (> 30 days) were due to cardiac disease in 13 patients in Group I and 22 patients in Group II. 3 patients (Group I) and 8 patients (Group

I) required reoperation at 1.4 ± 0.5 year after the first cardiac surgical procedure. Three patients (Group I) underwent successful renal transplantation 2.2 ± 0.4 years after CABG. Of the 34 surviving patients (Group I), 31 were free from anginal pain, 2 had stable angina and 1 had unstable angina at follow-up.

Table 6. Univariate analysis of pre and perioperative data between survived and deceased hemodialysed patients undergoing coronary artery bypass grafting procedure

	Failed (N=6)	Successful (N=50)	P
Cerebrovascular disease	5	18	0.04
Left ventricular ejection fraction	33±3	39±3.5	0.001
Hemodialysis duration	5.1±1.3	2.8±0.8	0.0017

Discussion

Almost 40-50% of deaths in HD patients can be attributed to coronary artery disease (4,15). It still remains unclear whether the progress of coronary artery disease is accelerated in dialysed patients compared to the general population (5,8,9). Other studies proposed that cardiac disorders might be aggravated by renal disease itself or by comorbid findings (16) associated with end-stage renal disease. Also, valvular, coronary arteries and conduction system calcification may be accelerated in HD patients (11) and septic events such as endocarditis may be regarded as typical complication from long-term HD (3,5). Recently, series have been published

but reports on long-term results after cardiac intervention are scarce (1-6,8,11,12,17-18,22). Most of these series were not uniformly studied because of different profiles and cardiac pathologies. It is difficult to compare all the studies because the inclusion criteria are inconsistent.

The tolerance of cardiopulmonary bypass procedures is conceivably reduced in the absence of renal function because of the patient's inability to cope with massive fluid shifts in the different body components induced by the cardiopulmonary bypass. Multiple comorbid disorders found in this pool of patients predispose them to increased operative mortality and

morbidity, including platelet dysfunction, and especially susceptibility to infection (3-4,10). Some authors recommend HD more than 24 hours before the cardiopulmonary bypass procedure, others advocate the use of intraoperative HD (19). We preferred intraoperative hemofiltration which permits to achieve an acceptable control of water and electrolyte (mainly

K+) balance until maintenance HD could be resumed. The HCT was raised to 30% with transfusion before surgery if necessary. In HD patients with depressed left ventricular function the peritoneal dialysis was instituted after the surgical procedure due to the advantages of avoiding hemodynamic instability that it offers.

Table 7. In-hospital mortality of hemodialysed patients undergoing coronary artery bypass grafting procedure (Literature review since 1990)

First Author	Year	Total	Mortality
1. Batiuk	1991	25	4 (16%)
2. Ko	1993	25	4(16%)
3. Owen	1994	21	2 (9%)
4. Blum	1994	40	6 (15%)
5. Garrido	1995	15	4 (27%)
6. Ashraf	1995	48	8 (17%)
7. Shibuya	1996	36	1 (2.8%)
8. Samuels	1996	13	4 (31%)
9. Nakayama	1997	54	4 (7.4%)
10. Christiansen	1997	22	4 (18%)
11. Kanzai	1998	14	-
12. Durmaz	1999	8	1 (12.5%)
13. Frenken	1999	45	2 (4.5%)
14. Khaitan	2000	70	10 (14.3%)
15. Prifti	2000	56	6 (10.5%)
Total		492	50/492 (12%)

In our series, the hospital mortality in HD patients was higher but not significant versus CRF non HD patients. Other studies demonstrated a higher postoperative mortality in HD patients (Table 7). Such studies revealed a postoperative mortality from 3% to 31% (mean 12%).

The postoperative complications were significantly higher in HD patients compared to CRF non HD patients undergoing CABG procedure. The propensity to infection in HD patients is attributed to decreased leukocyte chemotaxis and leukopenia (20). The accelerated atherosclerosis and diffuse cholesterol embolization syndrome (7) are manifested by cerebrovascular or other visceral vessel complications. The presence of a significantly higher incidence of preoperative AMI associated with a considerable

number of patients with triple vessel disease and heavily calcified lesions of the coronary arteries confirm the presence of an accelerated atherosclerosis in HD patients. The necessity of inotropes' use in the postoperative course was significantly higher in the study group versus control group patients. Such data demonstrated that CRF patients in general and HD patients specifically, are at a substantial risk of experiencing important cardiac complications.

The creatinine level increased significantly after CABG compared to the preoperative data in CRF non HD patients. 64 patients required postoperative HD. This means that the status of CRF non HD patients worsened significantly following CABG procedure, requiring postoperative HD.

We found a higher incidence of preoperative non cardiac comorbid features in CRF patients compared to patients with normal renal functions and in HD patients versus CRF non HD patients. Pepper et al (13) felt that the morbidity and late mortality in HD patients was heavily influenced by the non cardiac comorbid diseases. Rostand et al (14), found the old age as major factor affecting mortality. Samuels et al (7), revealed that age >70 years is the most important factor predicting mortality. Other studies revealed that NYHA class 4 (6) and cerebrovascular disease (5) are strong predictors of diminished long-term survival, which is better when the duration of HD is shorter (4). Nakayama et al (12) found a higher coronary calcification score in HD patients. Less than complete revascularization has also been addressed by Koyanagi et al (8) due to heavily calcified coronary arteries and poor vessel quality in HD patients. Recently, Khaitan et al (22), in their series of 70 HD patients undergoing CABG, found congestive heart failure, cardiomegaly and associated valve surgery as predictors for poor survival. In our series, strong predictors for poor overall survival in CRF non HD patients were found to be the cerebrovascular disease, AMI, LVEF <35% and CRF duration. The cerebrovascular disease, LVEF <35% and HD duration were found to be strong predictors for poor survival in HD patients. The CRF and HD duration seems to be strong preoperative predictors for poor short and long term outcome, probably due to the relation of CRF duration and comorbid features.

Only few researchers studied the long-term survival of HD patients and CRF non HD patients undergoing CABG. Samuels et al (7) found a 5% mortality at 30 months follow-up in CRF non HD patients undergoing CABG. Nakayama et al (12) found a 71% survival at 5 years follow-up in HD patients undergoing CABG. Khaitan et al (22) found a 40% survival at 3.5 years after CABG in HD patients. In our study, 5 years after surgery, only 68% of HD patients and 82.5% of CRF non HD patients were still alive. Some authors argue that

cardiac surgery does not alter the long-term survival of HD patients (17). Other studies revealed a mortality of 8% to 11% per year and an actuarial mortality of 40% after 5 years of in HD patients not undergoing cardiac surgery (21). A similar long-term survival in the population of patients operated and the general population indicates that such a therapeutic benefit exists, as the patients operated had proven coronary artery disease at the time of operation and conceivably a worse life expectancy than the HD general population. According to this data, CABG certainly improved the long term survival in HD patients. The long-term survival was significantly higher in CRF non HD patients than HD patients. Such data demonstrated that HD patients are at a substantial risk of a high long term mortality due to comorbid non-cardiac diseases such as: accelerated atherosclerosis, infectious risks due to HD, diabetes, cerebrovascular disease, hypertension; and cardiac comorbid findings such as: poor quality of coronary arteries inducing high incidence of AMI which results in a poor left ventricular function, important calcification of conduction system which induce malignant arrhythmias.

The long-term survival was significantly higher in HD patients undergoing arterial myocardial revascularization than CABG procedure using saphenous vein. CABG certainly does not affect the aggressive nature of atherosclerosis in this pool of patients, implying that long term graft patency can be expected to be lower than in non HD patients. Total arterial myocardial revascularization offered better long-term survival because of long-term arterial conduits patency over the saphenous vein.

Conclusion

CRF patients may undergo CABG with acceptable postoperative mortality and morbidity. Patients with presence of cerebrovascular disease, preoperative AMI, LVEF <35%, long history of CRF are at an increased risk for poor postoperative outcome. The HD patients undergoing CABG procedure have a higher postoperative mortality and are at a substantial

risk of experiencing postoperative major morbid events. LVEF <35% and long HD duration seems to increase the mortality in this pool of patients. A proper selection of HD patients, a robust study of coronary arteries quality, proper indications of surgical procedures and a good performance in effectuating myocardial revascularization in this pool of patients

are the necessary prerequisites for a successful surgical procedure. The coronary revascularization improves long-term survival in HD patients undergoing CABG procedure. Total arterial myocardial revascularization should be considered as the procedure of choice in HD patients offering better long-term outcome.

Conflicts of interest: None declared.

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